A123 CON

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants	:	James G. Barsoum et al.
Application No.	:	10/618,299 Confirmation No.: 6907
Filed	:	July 11, 2003
For	:	METHOD OF ENHANCING DELIVERY OF A THERAPEUTIC NUCLEIC ACID
Examiner	:	Not Yet Assigned
Group Art Unit	:	1653

New York, New York
February 24, 2004

Hon. Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

TRANSMITTAL LETTER FOR
INFORMATION DISCLOSURE STATEMENT

Sir:

Transmitted herewith is an Information Disclosure Statement (in duplicate) in the above-identified application, Form PTO-1449 (in duplicate) and documents cited therein. This Statement is submitted:

[ ] within three months of the application filing date;

[X] more than three months from the application filing date but before the mailing date of the first Office Action on the merits.

In accordance with 37 C.F.R. § 1.97, submission of this Statement requires no fee. However, if for any reason a fee is due, the Director is hereby authorized to charge payment of any fees required in connection with this Information Disclosure Statement to Deposit Account No. 06-1075. A duplicate copy of this letter is transmitted herewith.

Respectfully submitted,

James F. Haley, Jr. (Reg. No. 27,794)
Stanley D. Liang (Reg. No. 43,753)
Attorneys for Applicants
c/o FISH & NEAVE (Customer No. 1473)
1251 Avenue of the Americas
New York, New York 10020-1104
Tel.: (212) 596-9000
Fax.: (212) 596-9090

I hereby certify that this Correspondence is being deposited with the U.S. Postal Service as First Class Mail in an envelope Addressed to:
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450 on
February 24, 2004
Lillian Garcia
Lillian Garcia
Signature of Person Signing

A123 CON

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants	:	James G. Barsoum et al.
Application No.	:	10/618,299 Confirmation No.: 6907
Filed	:	July 11, 2003
For	:	METHOD OF ENHANCING DELIVERY OF A THERAPEUTIC NUCLEIC ACID
Examiner	:	Not Yet Assigned
Group Art Unit	:	1653

New York, New York
February 24, 2004

Hon. Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

INFORMATION DISCLOSURE STATEMENT

Sir:

Pursuant to 37 C.F.R. §§ 1.56 and 1.97, applicants hereby make of record the references listed below. Copies of these references are enclosed. A completed Form PTO-1449 listing all of the documents is enclosed herewith in duplicate.

United States Patents

Inventor	Patent No.	Issue Date
Higuchi et al.	3,710,795	January 16, 1973
Carter et al.	4,797,368	January 10, 1989
Kun et al.	5,262,564	November 16, 1993
Anderson et al.	5,399,346	March 21, 1995

Foreign Patent Applications

Publication No.	Publication Date	Country
WO 99/10516	March 4, 1999	PCT (WIPO)
WO 01/60377	August 23, 2001	PCT(WIPO)

Articles

R. Alemany, et al., "Blood Clearance Rates of Adenovirus Type 5 in Mice," *Journal of General Virology*, 81(11):2605-9 (2000).

D. Armentano, et al., "Effect of the E4 Region on the Persistence of Transgene Expression from Adenovirus Vectors," *Journal of Virology*, 71(3):2408-16 (1997).

N. B. Beck, et al., "Baculovirus Vectors Repress Phenobarbital-Mediated Gene Induction and Stimulate Cytokine Expression in Primary Cultures of Rat Hepatocytes," *Gene Therapy*, 7(15):1274-83 (2000).

C. A. Bradham, et al., "Activation of Nuclear Factor-KappaB During Orthotopic Liver Transplantation in Rats is Protective and Does Not Require Kupffer Cells," *Liver Transplantation and Surgery*, 5(4):282-93 (1999).

H. Chao, et al., "Several Log Increase in Therapeutic Transgene Delivery by Distinct Adeno-Associated Viral Serotype Vectors," *Molecular Therapy*, 2(6):619-623 (2000).

H. Chen, et al. "Persistence in Muscle of an Adenoviral Vector that Lacks All Viral Genes," *Proceedings of the National Academy of Sciences U.S.A.*, 94:1645-1650 (1997).

T. Daemen, et al., "Liposomal Doxorubicin-Induced Toxicity: Depletion and Impairment of Phagocytic Activity of Liver Macrophages," *International Journal of Cancer*, 61(5):716-721 (1995).

H. J. Delecluse, et al., "The Genetic Approach to the Epstein-Barr Virus: From Basic Virology to Gene Therapy," *Molecular Pathology*, 53(5):270-9 (2000).

O. Devergne, et al., "*In Vivo* Expression of IL-1 Beta and IL-6 Genes During Viral Infections in Human," *European Cytokine Network*, 2(3):183-94 (1991).

K. E. Drazan, et al., "Viral IL-10 Gene Therapy Inhibits TNF-Alpha and IL-1 Beta, Not IL-6, in the Newborn Endotoxemic Mouse," *Journal of Pediatric Surgery*, 31(3):411-4, (1996).

J. F. Engelhardt, et al., "Prolonged Transgene Expression in Cotton Rat Lung with Recombinant Adenoviruses Defective in E2a," *Human Gene Therapy*, 5(10):1217-29 (1994).

J. L. Goldstein, et al., "Defective Lipoprotein Receptors and Atherosclerosis. Lessons From an Animal Counterpart of Familial Hypercholesterolemia," *New England Journal of Medicine*, 309(5):288-96 (1983).

S. Hegenbarth, et al., "Liver Sinusoidal Endothelial Cells Are Not Permissive for Adenovirus Type 5," *Human Gene Therapy*, 11(3):481-6 (2000).

W.S. Hu, et al., "Design of Retroviral Vectors and Helper Cells for Gene Therapy," *Pharmacological Reviews*, 52(4):493-511 (2000).

S. Ishibashi, et al., "Hypercholesterolemia in Low Density Lipoprotein Receptor Knockout Mice and Its Reversal by Adenovirus-Mediated Gene Delivery," *Journal of Clinical Investigation*, 92(2):883-93 (1993).

S. Ishibashi, et al., "Massive Xanthomatosis and Atherosclerosis in Cholesterol-Fed Low Density Lipoprotein Receptor-Negative Mice," *Journal of Clinical Investigation*, 93(5):1885-93 (1994).

K. Jooss, et al., "Cyclophosphamide Diminishes Inflammation and Prolongs Transgene Expression Following Delivery of Adenoviral Vectors to Mouse Liver and Lung," *Human Gene Therapy*, 7(13):1555-66 (1996).

K. Jooss, et al., "Blunting of Immune Responses to Adenoviral Vectors in Mouse Liver and Lung with CTLA4Ig," *Gene Therapy,* 5(3): 309-319 (1998).

M. Kay, et al., "Transient Immunomodulation with anti-CD40 Ligand Antibody and CTLA4Ig Enhances Persistence and Secondary Adenovirus-Mediated Gene Transfer into Mouse Liver," *Proceedings of the National Academy of Sciences U. S A.*, 94: 4686-4691 (1997).

M. A. Kay, et al., "Viral Vectors for Gene Therapy: The Art of Turning Infectious Agents Into Vehicles of Therapeutics," *Nature Medicine*, 7(1):33-40 (2001).

N. Kuriyama, et al., "Pretreatment with Protease is a Useful Experimental Strategy for Enhancing Adenovirus-Mediated Cancer Gene Therapy," *Human Gene Therapy*, 11(16):2219-30 (2000).

A. Lieber, et al., "The Role of Kupffer Cell Activation and Viral Gene Expression in Early Liver Toxicity after Infusion of Recombinant Adenovirus Vectors," *Journal of Virology*, 71(11):8798-8807 (1997).

A. Lieber, et al., "Inhibition of NF-KappaB Activation in Combination with Bcl-2 Expression Allows for Persistence of First-Generation Adenovirus Vectors in the Mouse Liver," *Journal of Virology*, 72 (11):9267-77 (1998).

S. Longman, et al., "Accumulation of Protein-Coated Liposomes in an Extravascular Site: Influence of Increasing Carrier Circulation Lifetimes," *Journal of Pharmacology and Experimental Therapeutics*, 275(3):1177-1184 (1995).

N. Morral, et al., "High Doses of a Helper-Dependent Adenoviral Vector Yield Supraphysiological Levels of Alpha1-Antitrypsin with Negligible Toxicity," *Human Gene Therapy*, 9(18):2709-16 (1998).

X. Q. Qin, et al. "Interferon-β Gene Therapy Inhibits Tumor Formation and Causes Regression of Established Tumors in Immune-Deficient Mice," *Proceedings of the National Academy of Sciences U.S.A.*, 95:14411-14416 (1998).

M. J. Parr, et al., "The Presence of G_{M1} in Liposomes with Entrapped Doxorubicin Does Not Prevent RES Blockade," *Biochimica et Biophysica Acta*, 1168(2):249-252 (1993).

G. Schieder, et al., "Genomic DNA Transfer with a High-Capacity Adenovirus Vector Results in Improved *In Vivo* Gene Expression and Decreased Toxicity," *Nature Genetics*, 18(2):180-3 (1998).

W. M. Siders, et al., "T Cell- and NK Cell-Independent Inhibition of Hepatic Metastases by Systemic Administration of an IL-12-Expressing Recombinant Adenovirus," *The Journal of Immunology*, 160:5465-5474 (1998).

N. Somia and I.M. Verma, "Gene Therapy: Trials and Tribulations," *Nature Reviews Genetics*, 1(2):91-9 (2000).

K. Tanzawa, et al., "WHHL-Rabbit: A Low Density Lipoprotein Receptor-Deficient Animal Model For Familial Hypercholesterolemia," *FEBS Letters*, 118(1):81-4 (1980).

N. Tao, et al., "Sequestration of Adenoviral Vector by Kupffer Cells Leads to a Nonlinear Dose Response of Transduction in Liver," *Molecular Therapy: The Journal of the American Society of Gene Therapy*, 3(1):28-35 (2001).

W. M. Tsui, et al., "Liver Changes in Reactive Haemophagocytic Syndrome," *Liver*, 12(6):363-7 (1992).

V. W. van Beusechem, et al., "Recombinant Adenovirus Vectors with Knobless Fibers for Targeted Gene Transfer," *Gene Therapy*, 7(22):1940-6 (2000).

N. van Rooijen, et al., "Transient Suppression of Macrophage Functions by Liposome-Encapsulated Drugs," *Trends in Biotechnology*, 15(5):178-185 (1997).

S. Wang, et al., "Effect of Clodronate on Macrophage Depletion and Adenoviral-Mediated Transgene Expression in Salivary Glands," *Journal of Oral Pathology and Medicine*, 28(4):145-51 (1999)

J. M. Wilson, et al., "Cystic Fibrosis. Vehicles for Gene Therapy." *Nature*, 365(6448):691-2 (1993).

G. Wolff, et al., "Enhancement of *In Vivo* Adenovirus-Mediated Gene Transfer and Expression by Prior Depletion of Tissue Macrophages in the Target Organ," *Journal of Virology*, 71(1):624-9 (1997).

Applicants respectfully request that the above-cited documents be (1) fully considered by the Examiner during the course of the examination of this application and (2) printed on any patent issuing from this application. Applicants also request that a copy of the enclosed Form PTO-1449, duly initialed by the Examiner, be forwarded to the undersigned with the next official communication.

Respectfully submitted,

James F. Haley, Jr. (Reg. No. 27,794)
Stanley D. Liang (Reg. No. 43,753)
Attorneys for Applicants
c/o FISH & NEAVE (Customer No. 1473)
1251 Avenue of the Americas
New York, New York 10020-1104
Tel.: (212) 596-9000
Fax.: (212) 596-9090

I hereby certify that this Correspondence is being deposited with the U.S. Postal Service as First Class Mail in an envelope Addressed to: Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450 on

February 24, 2004

Lillian Garcia

Signature of Person Signing

FORM PTO-1449 U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTY. DOCKET NO. A123 CON	SERIAL NO. 10/618,299
INFORMATION DISCLOSURE STATEMENT BY APPLICANT	APPLICANT James G. Barsoum et al.	CONFIRMATION NO. 6907
	FILING DATE 07/11/03	GROUP 1653

U.S. PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	3,710,795	01/16/73	Higuchi et al.	128	260	
	4,797,368	01/10/89	Carter et al.	435	320	
	5,262,564	11/16/93	Kun et al.	562	430	
	5,399,346	03/21/95	Anderson et al.	424	93.21	

FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES	TRANSLATION NO
	WO 99/10516	03/04/99	PCT (WIPO)	C12N	15/86		
	WO 01/60377	08/23/01	PCT (WIPO)	A61K	31/66		

EXAMINER DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not conformance and not considered. Include copy of this form with next communication to applicant.

FORM PTO-1449 U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTY. DOCKET NO. A123 CON	SERIAL NO. 10/618,299
INFORMATION DISCLOSURE STATEMENT BY APPLICANT	APPLICANT James G. Barsoum et al.	CONFIRMATION NO. 6907
	FILING DATE 07/11/03	GROUP 1653

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

EXAMINER INITIAL	
	R. Alemany, et al., "Blood Clearance Rates of Adenovirus Type 5 in Mice," *Journal of General Virology*, 81(11):2605-9 (2000).
	D. Armentano et al., "Effect of the E4 Region on the Persistence of Transgene Expression from Adenovirus Vectors," *Journal of Virology*, 71(3):2408-16 (1997).
	N. B. Beck, et al., "Baculovirus Vectors Repress Phenobarbital-Mediated Gene Induction and Stimulate Cytokine Expression in Primary Cultures of Rat Hepatocytes," *Gene Therapy*, 7(15):1274-83 (2000).
	C. A. Bradham, et al., "Activation of Nuclear Factor-KappaB During Orthotopic Liver Transplantation in Rats is Protective and Does Not Require Kupffer Cells," *Liver Transplantation and Surgery*, 5(4):282-93 (1999).
	H. Chao, et al., "Several Log Increase in Therapeutic Transgene Delivery by Distinct Adeno-Associated Viral Serotype Vectors," *Molecular Therapy*, 2(6):619-623 (2000).
	H. Chen, et al. "Persistence in Muscle of an Adenoviral Vector that Lacks All Viral Genes," *Proceedings of the National Academy of Sciences U.S.A.*, 94:1645-1650 (1997).
	T. Daemen, et al., "Liposomal Doxorubicin-Induced Toxicity: Depletion and Impairment of Phagocytic Activity of Liver Macrophages," *International Journal of Cancer*, 61(5):716-721 (1995).
	H. J. Delecluse, et al., "The Genetic Approach to the Epstein-Barr Virus: From Basic Virology to Gene Therapy," *Molecular Pathology*, 53(5):270-9 (2000).
	O. Devergne, et al., "*In Vivo* Expression of IL-1 Beta and IL-6 Genes During Viral Infections in Human," *European Cytokine Network*, 2(3):183-94 (1991).
	K. E. Drazan, et al., "Viral IL-10 Gene Therapy Inhibits TNF-Alpha and IL-1 Beta, Not IL-6, in the Newborn Endotoxemic Mouse," *Journal of Pediatric Surgery*, 31(3):411-4, (1996).
	J. F. Engelhardt, et al., "Prolonged Transgene Expression in Cotton Rat Lung with Recombinant Adenoviruses Defective in E2a," *Human Gene Therapy*, 5 (10):1217-29 (1994).
	J. L. Goldstein, et al., "Defective Lipoprotein Receptors and Atherosclerosis. Lessons From an Animal Counterpart of Familial Hypercholesterolemia," *New England Journal of Medicine*, 309(5):288-96 (1983).

EXAMINER DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not conformance and not considered. Include copy of this form with next communication to applicant.

FORM PTO-1449 U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTY. DOCKET NO. A123 CON	SERIAL NO. 10/618,299
INFORMATION DISCLOSURE STATEMENT BY APPLICANT	APPLICANT James G. Barsoum et al.	CONFIRMATION NO. 6907
	FILING DATE 07/11/03	GROUP 1653

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

EXAMINER INITIAL	
	S. Hegenbarth, et al., "Liver Sinusoidal Endothelial Cells Are Not Permissive for Adenovirus Type 5," *Human Gene Therapy*, 11(3):481-6 (2000).
	W. S. Hu, et al., "Design of Retroviral Vectors and Helper Cells for Gene Therapy," *Pharmacological Reviews*, 52(4):493-511 (2000).
	S. Ishibashi, et al., "Hypercholesterolemia in Low Density Lipoprotein Receptor Knockout Mice and Its Reversal by Adenovirus-Mediated Gene Delivery," *Journal of Clinical Investigation*, 92(2):883-93 (1993).
	S. Ishibashi, et al., "Massive Xanthomatosis and Atherosclerosis in Cholesterol-Fed Low Density Lipoprotein Receptor-Negative Mice," *Journal of Clinical Investigation*, 93(5):1885-93 (1994).
	K. Jooss, et al., "Cyclophosphamide Diminishes Inflammation and Prolongs Transgene Expression Following Delivery of Adenoviral Vectors to Mouse Liver and Lung," *Human Gene Therapy*, 7(13):1555-66 (1996).
	K. Jooss, et al., "Blunting of Immune Responses to Adenoviral Vectors in Mouse Liver and Lung with CTLA4Ig," *Gene Therapy,* 5(3): 309-319 (1998).
	M. A. Kay, et al., "Transient Immunomodulation with anti-CD40 Ligand Antibody and CTLA4Ig Enhances Persistence and Secondary Adenovirus-Mediated Gene Transfer into Mouse Liver," *Proceedings of the National Academy of Sciences U. S. A.*, 94: 4686-4691 (1997).
	M. A. Kay, et al., "Viral Vectors for Gene Therapy: The Art of Turning Infectious Agents Into Vehicles of Therapeutics," *Nature Medicine*, 7(1):33-40 (2001).
	N. Kuriyama, et al., "Pretreatment with Protease is a Useful Experimental Strategy for Enhancing Adenovirus-Mediated Cancer Gene Therapy," *Human Gene Therapy*, 11(16):2219-30 (2000).
	A. Lieber, et al., "The Role of Kupffer Cell Activation and Viral Gene Expression in Early Liver Toxicity after Infusion of Recombinant Adenovirus Vectors," *Journal of Virology*, 71(11):8798-8807 (1997).

EXAMINER DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not conformance and not considered. Include copy of this form with next communication to applicant.

FORM PTO-1449 U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTY. DOCKET NO. A123 CON	SERIAL NO. 10/618,299
INFORMATION DISCLOSURE STATEMENT BY APPLICANT	APPLICANT James G. Barsoum et al.	CONFIRMATION NO. 6907
	FILING DATE 07/11/03	GROUP 1653

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

EXAMINER INITIAL	
	A. Lieber, et al., "Inhibition of NF-KappaB Activation in Combination with Bcl-2 Expression Allows for Persistence of First-Generation Adenovirus Vectors in the Mouse Liver," *Journal of Virology*, 72 (11):9267-77 (1998).
	S. Longman, et al., "Accumulation of Protein-Coated Liposomes in an Extravascular Site: Influence of Increasing Carrier Circulation Lifetimes," *Journal of Pharmacology and Experimental Therapeutics*, 275(3):1177-1184 (1995).
	N. Morral, et al., "High Doses of a Helper-Dependent Adenoviral Vector Yield Supraphysiological Levels of Alpha1-Antitrypsin with Negligible Toxicity," *Human Gene Therapy*, 9(18):2709-16 (1998).
	X. Q. Qin, et al. "Interferon-β Gene Therapy Inhibits Tumor Formation and Causes Regression of Established Tumors in Immune-Deficient Mice," *Proceedings of the National Academy of Sciences U. S. A.*, 95:14411-14416 (1998).
	M. J. Parr, et al., "The Presence of G_{M1} in Liposomes with Entrapped Doxorubicin Does Not Prevent RES Blockade," *Biochimica et Biophysica Acta*, 1168(2):249-252 (1993).
	G. Schieder, et al., "Genomic DNA Transfer with a High-Capacity Adenovirus Vector Results in Improved *In Vivo* Gene Expression and Decreased Toxicity," *Nature Genetics*, 18(2):180-3 (1998).
	W. M. Siders, et al., "T Cell- and NK Cell-Independent Inhibition of Hepatic Metastases by Systemic Administration of an IL-12-Expressing Recombinant Adenovirus," *The Journal of Immunology*, 160:5465-5474 (1998).
	N. Somia and I. M. Verma, "Gene Therapy: Trials and Tribulations," *Nature Reviews Genetics*, 1(2):91-9 (2000).
	K. Tanzawa, et al., "WHHL-Rabbit: A Low Density Lipoprotein Receptor-Deficient Animal Model For Familial Hypercholesterolemia," *FEBS Letters*, 118(1):81-4 (1980).
	N. Tao, et al., "Sequestration of Adenoviral Vector by Kupffer Cells Leads to a Nonlinear Dose Response of Transduction in Liver," *Molecular Therapy: The Journal of the American Society of Gene Therapy*, 3(1):28-35 (2001).
	W. M. Tsui, et al., "Liver Changes in Reactive Haemophagocytic Syndrome," *Liver*, 12(6):363-7 (1992).

EXAMINER DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not conformance and not considered. Include copy of this form with next communication to applicant.

FORM PTO-1449 U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE INFORMATION DISCLOSURE STATEMENT BY APPLICANT	ATTY. DOCKET NO. A123 CON	SERIAL NO. 10/618,299
	APPLICANT James G. Barsoum et al.	CONFIRMATION NO. 6907
	FILING DATE 07/11/03	GROUP 1653

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

EXAMINER INITIAL	
	V. W. van Beusechem, et al., "Recombinant Adenovirus Vectors with Knobless Fibers for Targeted Gene Transfer," *Gene Therapy*, 7 (22):1940-6 (2000).
	N. van Rooijen, et al., "Transient Suppression of Macrophage Functions by Liposome-Encapsulated Drugs," *Trends in Biotechnology*, 15(5):178-185 (1997).
	S. Wang, et al., "Effect of Clodronate on Macrophage Depletion and Adenoviral-Mediated Transgene Expression in Salivary Glands," *Journal of Oral Pathology and Medicine*, 28(4):145-51 (1999)
	J. M. Wilson, et al., "Cystic Fibrosis. Vehicles for Gene Therapy." *Nature*, 365(6448):691-2 (1993).
	G. Wolff, et al., "Enhancement of *In Vivo* Adenovirus-Mediated Gene Transfer and Expression by Prior Depletion of Tissue Macrophages in the Target Organ," *Journal of Virology*, 71(1):624-9 (1997).

EXAMINER DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not conformance and not considered. Include copy of this form with next communication to applicant.